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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,178	01/24/2002	Kit S. Lam	8141/9886	5311

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Audrey A. Millemann
Weintraub Genshlea Chediak Sproul Law Corporation
11th Floor
400 Capitol Mall
Sacramento, CA 95814

EXAMINER	
EPPERSON, JON D	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,178	LAM ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,13 and 16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10 and 13* is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *10/13/06*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed November 15, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 10, 11, 13, 14 and 16-20 were pending. Applicants amended claims 10 and 13. Applicants also canceled claims 11 and 14. Therefore, claims 10, 13, and 16-20 are currently pending.

4. Please note that the prior art search has been extended in view of Applicants' amendments (which overcame the prior rejections listed in the 6/15/06 non-final office action) in accordance with MPEP § 803.02. As a result, all previous species elections requirements are hereby withdrawn. In view of the above noted withdrawal of the restriction requirement as to the linked species, applicant(s) are advised that if any claim(s) depending from or including all the limitations of the allowable generic linking claim(s) be presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. Therefore, claims 10, 13, and 16-20 are currently pending and examined on the merits (i.e., claims 16-20 are no longer withdrawn).

Withdrawn Objections/Rejections

6. The Hammond 35 U.S.C. § 103(a) rejection is withdrawn in view of Applicants' arguments (e.g., see 11/15/06 response, pages 8-9, section A) and accompanying 37 CFR 1.132 declaration by Alan L. Lehman (e.g., see Lehman 11/15/06 declaration, especially paragraphs 3 and 4).

New Rejections

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 16, 18-20 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicant's claims are directed to a broad genus of methods for identifying ligands that bind to a target (e.g., see independent claim 16, "A method for identifying a ligand specific for a target molecule ... ."). The method employs the use of a "label binder" to aid in a first marking step (e.g., see independent claims 16, "incubating a combinatorial library of solid phase supports with a label binder ... ."). No common structural features are provided for said label binder. That is, the claims and specification defines this term functionally without limiting the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form these label binders. Thus, Applicant's claims encompass the entire universe of label binders without exception i.e., virtually an infinite number of structurally diverse compounds.

In contrast, Applicant's specification sets forth only a handful of examples that do not share any common structural elements and/or properties (e.g., see specification, paragraph 20, wherein streptavidin-alkaline phosphatase conjugate, antiflag antibody, etc. are the label binders).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). Furthermore, a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." (e.g., see *University of*

California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)). Here, Applicant has failed to provide a definition, structure, formula or chemical name for any of the label binders. The CAFC has stated that a genus, which is set forth only in functional terms, "... is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function" (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (1997)). Here, Applicant's claimed methods employ label binders that can only be distinguished from other compounds by their function (i.e., their ability to act as a label binder). This was held to be impermissible in *Lilly*. Just as the generic term "cDNA" did not provide an adequate written description for the broad class of mammalian or vertebrate insulin DNA in *Lilly*, neither does the generic term "label binder" provide an adequate written description for this broad class of screening molecules because the term "label binder" only defines what the compound does (i.e., it ability to act as a label binder) rather than what it is (i.e., a molecular formula). In fact, this case is even more egregious than *Lilly* because there is no "genetic code" to correlate the structure with the function.

Furthermore, the general knowledge and level of skill in the art do not supplement the omitted description because no known structure/function relationship and/or chemical properties exists that could otherwise be used to show possession of the enormous genus. In addition, there is no known generally accepted method for producing this wide array of label binders. See MPEP § 2163.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claim 18** recites the limitation "said labeling" in the first line. There is insufficient antecedent basis for this limitation in the claim. Here, claim 16 from which claim 18 depends recites several "labeling" processes including labeling of the target, labeling with the label binder, etc. and, as a result, it is unclear which labeling Applicants are referring to.

B. **Claim 18** recites the limitation "the use of an antigen" in the last two lines. There is insufficient antecedent basis for this limitation in the claim.

C. ***Claim 18*** is vague and indefinite because it attempts to claim a process (i.e., a "labeling" process) without setting forth any steps involved in the process. For example, a claim which read: "A process for using monoclonal antibodies of claim 4 to isolate and purify human fibroblast interferon." was held to be indefinite because it merely recites a use without any active, positive steps delimiting how this use is actually practiced. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986). See also MPEP 2173.05(q). Here, claim 18 similarly recites a use antigen and corresponding antibody without reciting any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

9. Claims 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hammond (WO 01/40265 A2) (Date of Patent is **June 7, 2001**).(Filing Date is **December 2, 1999**) (5/29/03 IDS) in view of Tizard et al. (Tizard et al. "DiffScreen: the merging of image subtraction and molecular genetics for the rapid analysis of differentially screened cDNA libraries" *CABIOS* **1994**, *10(2)*, 209-210) (12/13/02 IDS) and Lam et al. (Lam et al., "Application of a dual color detection scheme in the screening of a random combinatorial peptide library" Journal of Immunological Methods **1995**, 180, 219-213).

For ***claims 16, 19 and 20***, Hammond et al. (see entire document) disclose methods for identifying ligands to a target molecule (e.g., see Hammond et al., abstract), which renders obvious the claimed invention. For example, Hammond discloses (1) incubating a combinatorial library of solid phase supports with a label binder (e.g., see pages 17-20, Example 1, especially page 17 wherein a combinatorial library of peptides is disclosed attached to solid phase "bead" supports; see also page 18, middle paragraph wherein a labeled secondary antibody is disclosed that contains phosphatase as the label binder). In addition, Hammond discloses (2) performing a first marking step to mark those of said solid phase supports that have a molecule of said label binder bound to them (e.g., see page 18, second to last paragraph wherein the phosphatase chemiluminescent substrate is disclosed to "mark" those beads that contain the primary and secondary antibody). Hammond also discloses (3) introducing said target molecule to said combinatorial library and incubating said combinatorial library with said target molecule (e.g., see page 19, paragraph 2, especially lines 10-12, "To detect beads containing a

peptide that binds specifically to the target, the above procedure of blocking and probing is duplicated except that the target is present in the two hour binding incubation."). This would also include "labeling the target molecule" as described above with a secondary antibody and a similar marking procedure with a chemiluminescent substrate. In addition, Hammond disclose obtaining a first image showing as marked those of said solid phase supports that were marked in said first marking step (e.g., see paragraph bridging pages 18 and 19 wherein a first "star map" is produced). Hammond also discloses performing a second marking step to mark those of said solid phase support that have a target molecule bound to them and obtaining a second image showing as marked those of said solid phase supports that have a target molecule bound to them (e.g., see page 19, lines 14-21). Hammond also discloses isolating one of said solid phase supports to determine the chemical structure of a ligand on one of said isolated solid phase supports (e.g., see page 19, second to last paragraph, "The beads are then loaded into a protein sequencer and the ligands on the positive beads are characterized by Edman degradation").

For ***claim 18***, Hammond discloses labeling via an antigen and the corresponding antibody (e.g., see Example 1 wherein both a primary and a second antibody are used; see also page 10, lines 20-23, "In general any probe molecule can be used ... e.g., an antibody"; see also 35 U.S.C. § 112, second paragraph rejection above).

The prior art teachings of Hammond differ from the claimed invention as follows:

For ***claims 16, 19 and 20***, Hammond fails to disclose creating a third image identifying those of said solid phase supports that have a target molecule bound to them

wherein said third image is created by comparing said first image and said second image. Hammond only discloses comparing the two marked libraries (e.g., see Hammond, page 19, lines 14-16).

For ***claim 17***, Hammond fails to disclose labeling via biotinylation and further wherein said label binder is a streptavidin alkaline phosphatase conjugate. Hammond discloses label binders like secondary antibodies conjugated to phosphatase.

However, the combined references of Tizard et al. and Lam et al. teach the following limitations that are deficient in Hammond:

For ***claims 16, 19 and 20***, the combined references of Tizard et al. and Lam et al. (see entire documents) teach the use of imaging techniques that employs obtaining a fist and second image and then subtracting said images on a pixel-by-pixel basis to create a third image (e.g., see Tizard et al., figure 1, see especially image (c), which represents the "third" image that is produced by subtracting said first and second images) including a B-A on a pixel-by-pixel basis (e.g., see Tizard et al., page 209, column 2).

For ***claim 17***, the combined references of Tizard et al. and Lam et al. disclose the use of biotin/streptavidin-AP.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the DiffScreen imaging techniques as taught by the combined references of Tizard et al. and Lam et al. to monitor the two sets of target/ligand libraries as disclosed by Hammond because Tizard et al., for example, explicitly state that the imaging system can be used to monitor two sets of DNA libraries (e.g., see Tizard et al., page 209, see also figure 1), which falls within the "nucleic acid"

screening embodiment disclosed by Hammond (e.g., see Hammond, page 6, last full paragraph, "In some embodiments ... the ligand molecules can be ... nucleic acids"; see also page 7, line 6 wherein the target is a protein). Furthermore, a person of skill in the art would have been motivated to use the DiffScreen imaging technique because it greatly reduces the time spent comparing two sets of libraries by avoiding tedious visual analysis and comparison (e.g., see Tizard et al., page 210; see also figure 1, especially figure 1(c) "subtracted image"), which is exactly the problem faced by Hammond (e.g., see Hammond, page 6, paragraph 1, step (g); see also page 11, fist full paragraph, "Subtraction of the first set of signals from the second reveals a set of signals that corresponds to beads that contain ligands that bind specifically to the target"). Finally, a person of ordinary skill in the art would reasonably have expected to be successful because both references disclose the use of autoradiography to image their library members (e.g., compare Tizard, figure 1 to Hammond, page 10, last full paragraph) and the technique does not depend on the nature of the library (e.g., plaques, colonies, solid-phase beads) but, rather, the nature and positioning of the labels (e.g., radioisotopes, fluorophores, etc.. In addition, Hammond states that their invention can be used with a wide range of ligands including polypeptide, polynucleotide, etc. (e.g., see Field of Invention).

In addition, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the biotin/streptavidin alkaline phosphatase conjugate as disclosed by the combined references of Tizard et al. and Lam et al. (e.g., see Lam et al., figure 1) for use in the marking steps because Hammond explicitly states

that "[b]inding of an agent or target to a ligand can be detected with a probe molecule by employing any art-recognized method"), which would encompass, for example, the art-recognized method of Lam et al. (e.g., see Lam et al., figure 1). Furthermore, a person of skill in the art would have been motivated to use the biotin/streptavidin-AP because it is very sensitive (e.g., see Lam et al., page 222, column 1, doesn't negatively impact library screening and can be combined with many different reagents for "dual color detection" to further eliminate false positives. Finally, a person of skill in the art would reasonably have expected to be successful because Lam et al. show that these reagents can be used to screen peptide libraries like the ones disclosed by Hammond.

Allowable Subject Matter

10. Claims 10 and 13 are allowed.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
February 18, 2007

JON EPPERSON
PRIMARY EXAMINER